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Association of BMI with Androgenic Hormones in Polycystic Ovarian Syndrome Patients

[*]Sakila.S[1], Muniappan.V[2], Santha.K[3], Balu Mahendran.K[3], Rajkumar.D[4]
1. Department of Physiology, Govt. Thiruvarur Medical College, Thiruvarur, Tamil Nadu, India.
2. Department of Anatomy, Rajah Muthiah Medical College and Hospital, Annamalai University, Annamalainagar, Tamil Nadu, India.
3. Department of Biochemistry, Rajah Muthiah Medical College and Hospital, Annamalai University, Annamalainagar, Tamil Nadu, India.
4. Department of Physiology, Rajah Muthiah Medical College and Hospital, Annamalai University, Annamalainagar, Tamil Nadu, India.

Abstract:
Background: *Polycystic ovary syndrome (PCOS) is the most common endocrine disorder amongst women of reproductive age and is associated with various metabolic perturbations, in addition to chronic anovulation and factors related to androgen excess.*
Aim: *The aim of this study was to evaluate association body mass index (BMI) with estrogen, testosterone, malondialdehyde and serum lipids in PCOS patients compared with healthy volunteers.*
Materials and methods: *Sixty patients of PCOS aged 25–35 years and 30 healthy age matched controls were selected as controls. Demographic details, family history and past medical history were obtained through interview by a physician. Anthropometric measurements included weight and height of the participants. The included patients were categorized into two groups according to the Asian reference values for BMI (Group I- ≤ 23 kg/m2, and Group II- >23kg/m2). Fasting glucose, total cholesterol, high-density lipoprotein (HDL), insulin, Malondialdehyde (MDA) and androgen levels were determined. IR was calculated using homeostasis model assessment for insulin resistance (HOMA-IR).*
Results: *The mean serum estrogen, testosterone, MDA levels were significantly increased in PCOS patient groups compared with controls. The group II patients showed significantly increased serum estrogen, testosterone, MDA levels compared to group I. In both the groups BMI positively correlated with estrogen, testosterone, MDA. In group II BMI showed positive correlation with serum Cholesterol, TGL, LDL and negative correlation with and HDL. In group I BMI showed positive correlation with triglycerides and LDL and there was no statistical significant correlation with HDL and total cholesterol.*
Conclusion: *Obesity and higher levels of estrogen and testosterone are strong risk factors for PCOS. Regular monitoring of estrogen and testosterone levels may help in reduction of long-term health consequences of PCOS.*
Keywords: *PCOS, BMI, Insulin resistance, Androgen hormones*

I. Introduction

Polycystic ovary syndrome (PCOS) is an endocrine-metabolic disorder characterized by multiple hormonal imbalances, reflecting on a clinical presentation dominated by manifestations of hyperandrogenism, which generate short and long term consequences on female health [1,2]. Although the diagnosis of PCOS is based exclusively on reproductive criteria (hyperandrogenism, oligo/anovulation, and/or PCO on ultrasound) and management tends to focus primarily on treatment of infertility and hirsutism [3]. PCOS women have an increased risk of presenting with insulin resistance (IR), impaired glucose tolerance (IGT) , type 2 diabetes mellitus (DM2), obesity and dyslipidemia [4-6]. These features, along with other alterations such as endothelial dysfunction and a chronic low-grade inflammatory state, underlie the greater risk of developing cardiovascular disease and increased all-cause mortality observed in these subjects [7]. Amongst the complications previously mentioned, obesity stands out as it has reached epidemic proportions, with a worldwide prevalence of 35% women are obese [8,9]. So the objective of the present study was to evaluate the association of body mass index with androgenic hormones and serum lipids in PCOS patients.

II. Materials And Methods

The study groups comprised 60 newly diagnosed PCOS patients aged between 25–35 years from the out-patient departments of Gynecology Rajah Muthiah Medical College and Hospital, Annamalai University, Annamalainagar, Tamil Nadu, India, were selected for the present study. The included patients were categorized into two groups according to the Asian reference values for BMI (Group I- ≤ 23 kg/m^2, and Group II-

>23kg/m^2)[10]. PCOS was diagnosed using the Rotterdam Criteria [11] which states that PCOS is diagnosed if patient have any two of the following three features, 1) oligo/amenorrhea and/or anovulation, 2) hyperandrogenism and/or hyperandrogenemia, and 3) polycystic ovaries on ultrasound after exclusion of other etiologies. Oligomenorrhea was defined as infrequent menstruation or less than 9 menstrual periods per year. Amenorrhea was defined as absence or abnormal cessation of menses for three months or more [11]. For diagnostic purposes, since we recruited already diagnosed patients of PCOS, presence of either clinical hyperandrogenism or biochemical hyperandrogenemia was considered acceptable, whichever used by the diagnosing gynecologist. Hyperandrogenism was defined as a score of 7 or more on the Ferriman Gallaway index, or apparent severe hirsutism, acne and alopecia [12]. We excluded pregnant PCOS patients, type 2 diabetes mellitus, chronic liver disease, thyroid dysfunction, and using medications such as steroids, contraceptives, hypoglycemic/antidiabetic drugs for this study. Thirty age-matched healthy females with BMI <23 kg/m^2 and regular menstrual cycle selected as controls. Females taking medication, including steroids and contraceptives were not included. The informed consent was obtained from the study subjects and the study was approved by the Institutional Human Ethics Committee (IHEC). Experiments were done in accordance with Helsinki declaration of 1975.

Biochemical analysis:

Fasting blood samples were obtained from the subjects immediately after enrolment. Blood samples were centrifuged at 2000×g for 10 min. Samples were analyzed for fasting blood glucose, lipid Profile(Total Cholesterol, HDL, Triglycerides), by using Auto analyzer. Serum estrogen, testosterone and insulin were assayed by Enzyme Linked Immuno Sorbent Assay (ELISA). Malondialdehyde (MDA) was measured by Thiobarbituric Acid Reactive Substances (TBARS) method [13].

Statistical analysis:

Statistical analyses were carried out with SPSS 20.0. Values were expressed as mean ± standard deviation, p value < 0.05 was considered statistically significant. Normally distributed data were analyzed by using one-way ANOVA. The Pearson correlation test was used for correlation analysis.

III. Results

Table 1: Baseline parameters in controls and PCOS Patients

Parameters	Controls (n=30)	Group I PCOS patients (n=30)	Group-II PCOS patients (n=30)
Age	25.7±3.8	26.8±2.8	25.9±5.5
Body mass index	21.76±1.67	22.19±1.44	27.09±3.46^{a*,b**}
Waist/Hip ratio	0.89± 0.037	0.91±0.08	0.96±.046 ^{b*}
Systolic BP (mm Hg)	121±7.3	128.3±9.2 ^{a*}	135.7±10.1 ^{a**,b*}
Diastolic BP (mm Hg)	80.4±6.3	83.1±9.4	87.4±6.8 ^{a**,b*}

Data are expressed as mean ±SD, **p<0.001,*p<0.05 was considered statistically significant.
a= comparison between Controls and Group I and Group II PCOS patients
b= comparison between Group I and Group II PCOS patients

Table 2: Estrogen, Testosterone, Lipid profile and MDA levels in controls and PCOS patients

Parameters	Controls (n=30)	Group I PCOS patients (n=30)	Group-II PCOS patients (n=30)
FastingPlasma glucose (mg/dl)	82.8±9.3	112.3±18.7 ^{a**}	132.3±15.5 ^{a**,b**}
HOMA-IR	1.29±0.17	2.37±0.13 ^{a**}	3.5±0.4 ^{a**,b**}
Estrogen (pg/ml)	145.6±10.9	191.5±15.4 ^{a**}	255.8±24.2 ^{a**,b**}
Total testosterone (ng/dl)	40.4±8.5	69.8±14.3 ^{a**}	78.3±12.5 ^{a**,b**}
Serum cholesterol (mg/dl)	156.3±9.2	187.1±15.4 ^{a**}	210.7±18.7 ^{b**,c**}
Serum Triglycerides (mg/dl)	97.6±14.5	137.5±39.4 ^{a**}	165.9±42.8 ^{a**,c*}
HDL cholesterol (mg/dl)	42.4±5.4	37.5±4.1 ^{a**}	37.7±3.9. ^{a**}
LDL cholesterol (mg/dl)	113.6±10.2	134.8±14.5 ^{a**}	148.1±29.4 ^{a**,b*}
Malondialdehyde (µ mol/L)	1.42±0.67	4.94±0.34 ^{a**}	5.74±0.76 ^{a**,b**}

Data are expressed as mean ±SD, **p<0.001,*p<0.05 was considered statistically significant.
a= comparison between Controls and Group I and Group II PCOS patients
b= comparison between Group I and Group II PCOS patients

Table 3: Correlation between BMI &measured parameters in PCOS patients

Parameters	Group-I PCOS patients	Group II PCOS patients
Estrogen	0.659**	0.738**
Testosterone	0.421*	0.543**
HOMA-IR	0.498**	0.522**

Cholesterol	0.201	0.547**
TGL	0.467**	0.823**
HDL	-0.131	-0.392*
LDL	0.482**	0.726**
Malondialdehyde	0.267	0.389*

Data values representing Correlation Coefficient(r)
**Correlation is significant at the 0.01 level (2-tailed).
*Correlation is significant at the 0.05 level (2-tailed).

IV. Discussion

PCOS is a heterogeneous syndrome associated with a wide range of endocrine and metabolic abnormalities, including hyperinsulinaemia, hyperglycemia, dyslipidemia and obesity, which are regarded as hallmark components of metabolic syndrome [14, 15]. While obesity is regarded as one of the putative factors leading to metabolic syndrome, the link between PCOS and metabolic syndrome would seem to be due to insulin resistance (IR) [16].

In the present study it has been observed that mean serum estrogen , testosterone and MDA levels are significantly increased in both groups of PCOS patients compared to control subjects. Among the groups mean serum estrogen, testosterone, HOMA-IR and MDA levels are significantly increased in group II patients (Obese) compared with group I (Non obese) PCOS patients. Apridonidze et al., [17] described a higher prevalence of hyperandrogenemia in women with concomitant PCOS and metabolic syndrome. In addition, there is an association between hyperandrogenemia and vascular dysfunction in PCOS [18]. This may reflect the insulin resistance and direct adverse effect of hyperandrogenemia [19]. The hyperandrogenism favors a central/visceral distribution pattern of body fat and primary contributor to the development of systemic insulin resistance [20]. Visceral fat has increased lipolytic activity and may result in relative increases of free fatty acids in PCOS, which in turn induce skeletal muscle insulin resistance [21, 22]. Insulin resistance is initially compensated for by hyperinsulinaemia through which normal glucose tolerance is preserved. However, over time further deterioration of glucose metabolism, by increased insulin resistance or by decreased compensatory insulin secretory responses or by both, accelerates the progression to impaired glucose tolerance and eventually to overt type 2 diabetes. Chronic hyperinsulinaemia exacerbates insulin resistance and contributes directly to β-cell failure and diabetes [23].

Dyslipidemia is observed in both obese and non-obese women with PCOS compared with age- and BMI-matched control women as reported earlier [24, 25]. The characteristic dyslipidemic profile (high triglycerides [TGs] and low high-density lipoprotein-cholesterol [HDL-C]) associated with insulin resistance is the most common metabolic abnormality in PCOS. In addition we observed BMI showed strong positive correlation with estrogen, testosterone, malondialdehyde, triglycerides and LDL cholesterol in both groups of PCOS patients, and in group II (obese PCOS) BMI showed positive correlation with total cholesterol and negative correlation with HDL. Oxidative stress and inflammation seem to contribute to hyperandrogenemia in PCOS. Several studies reported that oxidative stress and inflammatory markers were found to be positively correlated with androgen levels in PCOS patients [26-28]. Hyperandrogenemia seems to have the ability to cause obesity, dyslipidemia, IR and altered oxidative stress markers, such as malondialdehyde [29-32].

Obesity and higher levels of estrogen and testosterone are strong risk factors for PCOS. Regular monitoring of estrogen and testosterone levels may help in reduction of long-term health consequences of diagnosed PCOS women.

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